REMARKS

Claims 8-11, 15, 17-20, 22-25, 28, and 34-50 remain pending in this application. Claims 11 and 13 are currently amended. Support for the amendments can be found throughout the specification and claims as originally filed. No new matter has been added.

Applicants thank the Examiner for acknowledging the allowability of claims 8-10, 17-19, 22-24, 28, 44, 46, 49, and 50. Claim 13 was objected to for depending from a rejected base claim. Claim 13 has been rewritten in independent form and thus should also be allowable.

Specification

The specification was objected to for not disclosing SEQ ID NOs for the nucleic acid sequence disclosed on page 18, line 2. The specification is currently amended to add appropriate sequence identifiers at page 18 and at another place in the specification. No new matter has been added by these amendments.

Claim Objection

Claim 13 was objected to for depending from a rejected claim, but the Examiner indicated it would be allowable if rewritten in independent form. Claim 13 has been so amended to include all the limitations of claim 11. Applicants therefore request allowance of claim 13.

Rejections under Section 112, first paragraph

Claims 11, 15, 20, 25, 34-43, and 45 are again rejected under section 112, first paragraph, for alleged lack of enablement. Applicants strongly disagree for reasons of record. Further comments regarding the Examiner's arguments follow.

The Office action states, at page 3, that

> The Specification explicitly disclosed that **only the full length protein consisting of** amino acid sequence 1-149 of SEQ ID NO:1, encoded by nucleotides 294 through 740 of SEQ ID NO:2; or polypeptide **consisting** of amino acid sequences of residues 76 through 149 of SEQ ID NO:1 can inhibits the differentiation of

myoblasts into myotubes and can inhibit the activity of p53 (see Examples 8-11 in particular). [emphasis and textual irregularities in the original]

Applicants strongly disagree with the quoted statement. It is simply not true that Applicants taught that "only" polypeptides consisting of full length SEQ ID NO:1 or amino acid residues 76-149 of SEQ ID NO:1 can inhibit differentiation of myoblasts into myotubes and/or inhibit the activity of p53. Rather, the specification discloses that peptides comprising these sequences and peptides comprising sequences with identity to these sequences can also display these activities. At page 7, lines 1-18, the specification explicitly teaches that "[i]t is ... well within the art of a person with ordinary skill to obtain a protein functionally equivalent to the mouse striamin protein (SEQ ID NO:2) by isolating DNA showing significant homology with the DNA that encodes the mouse striamin protein (SEQ ID NO:1) or a part thereof." The specification describes the isolation of such DNA with significant homology and the production of functionally equivalent recombinant fusion proteins (pages 12-13). The specification also teaches, at page 5, line 22, to page 6, line 5, that "one skilled in the art can prepare modified proteins whose functions are equivalent to those of the native protein ... using ... well-known method[s] for modifying proteins." These techniques to obtain functionally equivalent proteins that are structurally related to an original protein are routine to persons skilled in the art.

The Examiner maintains that claim 11 reads on antisense nucleic acid, and that such an antisense sequence does not encode a striamin polypeptide or functional equivalent. Applicants point out that the functional limitation present in the claim ensures that the claim does not encompass a single stranded antisense nucleic acid, so the Examiner's fears are groundless. However, rather than argue the point, Applicants prefer to render it moot by amending claim 11 to recite that the nucleic acid is "double stranded."

Claims 11, 20, 25, and 34-42 were rejected under the contention that "the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed" (page 6). Applicants maintain that production and identification of the claimed variants are routine to one skilled in the art. As indicated above, the procedures to create variants of nucleic acids are well-known to skilled individuals. Additionally, the specification describes methods to identify variant nucleic acids encoding polypeptides that inhibit the differentiation of myoblasts into myotubes (see

pages 16-17 and Example 6). As stated in the previous response, Bowie et al. (Science 247:1306-1310, 1990) indicate that one can expect to find over half (and possibly well over half) of random substitutions in any given protein to result in mutated proteins with full or nearly full activity. The fact that it is theoretically possible to make variants that do not have this activity is irrelevant to the question of enablement, as it is always theoretically possible to create inoperative variants of claimed inventions—even in the mechanical arts. The proper question should be whether it would require undue experimentation to make any embodiments that meet the criteria of the claim. Since one can expect at least 50% of random substitutions to result in fully functional proteins, and the odds go even higher if the substitutions are non-random ones deliberately designed to minimize impact on the protein's activity (e.g., conservative substitutions, as described in the specification at page 6, lines 6-14), the answer to that question is, of course, that it would not require undue experimentation. It would be utterly routine to make variant nucleic acids, test the proteins encoded by the nucleic acids, and isolate those that inhibit the differentiation of myoblasts into myotubes. In view of the routine nature of these experiments and the extensive teachings in the specification, the rejection of these claims should be withdrawn.

Regarding the rejection of claim 15, the Examiner alleges that no working example of an antisense nucleic acid was disclosed in the specification. The Office action, at page 5, states that, "There is no teaching that expression of antisense strand inhibits the expression of steriamin-S. [The] examples only disclosed that in the cells wherein antisense strriamin has been expressed, the activity of p53 slightly increases, compare to the control" [misspellings and other non-standard English in the original]. Applicants grant that inhibition of striamin polypeptide expression was not demonstrated directly. Example 8 demonstrates that overexpression of striamin decreases p53 transcriptional activity 4.6-fold compared to the empty vector control (i.e., striamin inhibits p53 transcriptional activity). In a complementary experiment, Applicants expressed an antisense striamin construct in the same cells in an attempt to down-regulate striamin expression. The antisense striamin construct increased p53 activity by 1.6-fold compared to the vector control, consistent with decreased expression of a p53 inhibitor. The Examiner dismisses this 60% increase in p53 activity as merely "slight." However, the result was observable and replicated in quadruplicate experiments, indicating (though indirectly) that

the antisense construct was sufficient to decrease expression of striamin. The Office action further states, illogically and without elaboration, that "one skilled in the art would know that said results does not inherently interpreted as inhibition of the expression." However, the action provides no credible alternative explanation. Indeed, since antisense inhibition of expression is well recognized in the art, a decrease in striamin expression by the antisense construct is by far the most likely explanation for the increase in p53 activity observed. Therefore, Applicants maintain that the disclosure of Example 8 represents a working example of an antisense nucleic acid that inhibits expression of a striamin polypeptide.

Applicants disagree with the continued rejection of claims 43 and 45, based on the Examiner's allegation that "Applicant is relying on certain biological activities and the disclosure of a single species to support an entire genus." Applicants do not understand the Examiner's position. As the Examiner is doubtlessly aware, the binding activity of polypeptides is a result of the polypeptide's sequence and/or three-dimensional structure. That residues 1-75 and 76-149 of SEQ ID NO:1 could each bind to p53 when isolated indicates that each contains a sequence or structure responsible for binding to p53. Claims 43 and 45 require the presence of residues 1-75 or 76-149 of SEQ ID NO:1 in the encoded polypeptide. So, by definition, these claims are limited to nucleic acids encoding polypeptides with a structure shown to be capable of binding p53. Further, other species were disclosed in the specification: polypeptides comprising residues 1-75 or 76-149 of SEQ ID NO:1 and a hexahistidine peptide or green fluorescent protein (GFP) were produced (see Examples 10 and 11) and demonstrated to bind to p53 either *in vitro* or *in vivo*. Since the p53-binding activity of residues 1-75 or 76-149 is necessarily dependent upon the sequence and/or structure of these polypeptides, and since functional polypeptides comprising these residues are disclosed, it is apparent that claims 43 and 45 are fully enabled. The Examiner has provided no basis to believe otherwise.

Applicants request reconsideration and withdrawal of all pending enablement rejections for reasons of record and the arguments above.

Rejection under Section 102

Claims 47 and 48 were rejected under section 102(e) as allegedly anticipated by U.S. Patent 6,458,533. According to both the prior and the present Office actions, the '533 patent

teaches an isolated 60mer nucleic acid (SEQ ID NO:95) comprising 17 nucleotides that are 100% identical to nucleotides 541-557 of SEQ ID NO:2. As stated on page 16 of Applicants' response to the previous Office action, Applicants could not find SEQ ID NO:95 in the '533 patent; in fact, this patent includes only 32 sequences in its sequence listing. Despite Applicants' explicit request in the prior response, the Examiner still has provided no clarification as to the identity of the '533 patent's sequence that allegedly anticipates Applicants' claims. Accordingly, this rejection appears to be in error and should be withdrawn, resulting in the allowance of these two claims (there being no other ground stated for their rejection). If the Examiner intends to maintain the rejection, Applicants again request that the basis for it be explained so that Applicants have an opportunity to respond.

Applicants submit that all of the currently pending claims are allowable and request confirmation of such by the Examiner.

This Reply is submitted within two months of the timely filing of a Notice of Appeal. No extension or fees are due. Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 14875-066002.

Respectfully submitted,

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